

### Remarks

Claims 1 and 3-16 are currently pending. Claims 8-12, 15, and 16 stand withdrawn from consideration. Claims 1, 3, 6, and 7 have been amended. Claim 2 has been canceled without prejudice. Support for the claim amendments can be found in the specification and claims as originally filed. Therefore, no new matter has been added. The Applicants expressly reserve the right to prosecute further the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120 and § 121.

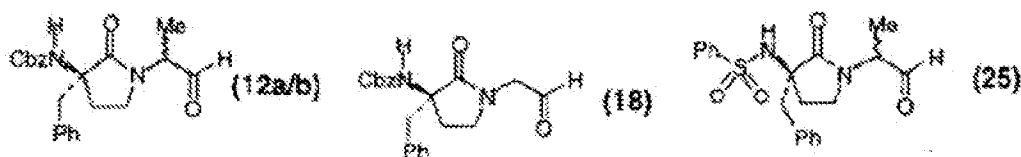
### Claim Rejections Based on 35 U.S.C. § 102

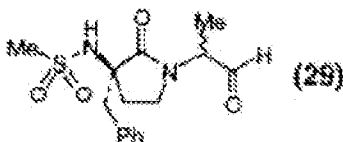
#### *Scheidt*

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Scheidt *et al.*, *Bioorganic and Medicinal Chemistry Letters* 6: 2477-2494 (1998) ("Scheidt"). The Applicants respectfully traverse.

To anticipate a claim under §102, a reference must teach each and every element of the claim, either expressly or inherently. M.P.E.P. § 2131. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union oil Co. of California*, 8144. F. 2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Furthermore, "[t]he identical invention must be shown in as complete detail as contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1566 (Fed. Cir. 1990). Applicants submit that the cited art does not meet this standard.

The Applicants have canceled claim 2 without prejudice. As to the remaining claims, the Examiner contends that Scheidt discloses that four compounds (depicted below) that anticipate the pending claims.





In the parlance of the structural limitations (i.e., formula I) of the rejected claims, the compounds disclosed by Scheidt have  $R^6$  defined as set forth below.

For compounds **12a/b**:  $R^6$  is  $-C(=O)R^{12}$ .

For compound **18**:  $R^6$  is  $-C(=O)R^{12}$ .

For compound **25**:  $R^6$  is  $-C(=O)R^{12}$ .

For compound **29**:  $R^6$  is  $-C(=O)R^{12}$ .

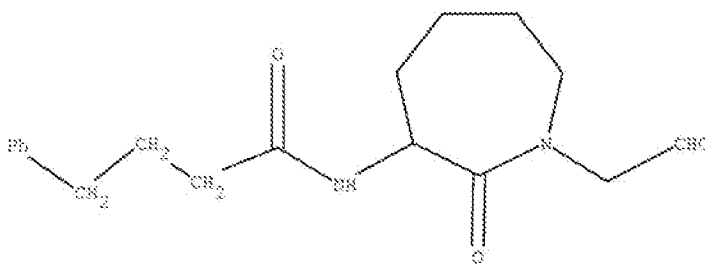
The Applicants have amended the claims to limit the definition of  $R^6$  to cyano, boronic acid,  $-SO_2Z^1$ ,  $-P(=O)Z^1$ ,  $-C(=NH)NH_2$ , or  $-CH=NR^{12}$ . Consequently, the Applicants respectfully assert that the amended claims do not read on any of the compounds disclosed in Scheidt.

#### *Giannessi*

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Giannessi *et al.*, EP Patent No. 0462949 ("Giannessi"). The Applicants respectfully traverse.

The criteria for determining whether a reference anticipates a claim are outlined above.

The Applicants have canceled claim 2. As to the remaining claims, the Examiner contends that Giannessi discloses that a compound (depicted below) that anticipates the pending claims.



In the parlance of the structural limitations (i.e., formula I) of the rejected claims, the compound disclosed by Giannessi has  $R^6$  defined as follows:  $R^6$  is  $-C(=O)R^{12}$ .

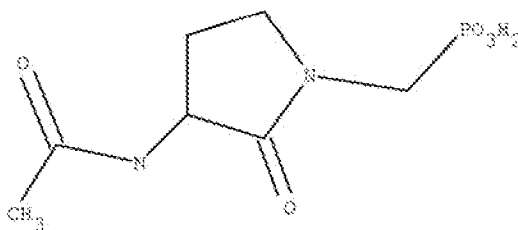
The Applicants have amended the claims to limit the definition of  $R^6$  to cyano, boronic acid,  $-SO_2Z^1$ ,  $-P(=O)Z^1$ ,  $-C(=NH)NH_2$ ,  $-CH=NR^{12}$ . Consequently, the Applicants respectfully assert that the amended claims do not read on the compound disclosed in Giannessi.

*Natchev*

Claims 1, 2 and 4-7 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Natchev, *Synthesis* **12**: 1079-1084 (1987) ("Natchev"). The Applicants respectfully traverse.

The criteria for determining whether a reference anticipates a claim are outlined above.

The Applicants have canceled claim 2. As to the remaining claims, the Examiner contends that Natchev discloses that a compound (depicted below) that anticipates the pending claims.



In the parlance of the structural limitations (i.e., formula I) of the rejected claims, the compound disclosed by Natchev has  $R^6$  defined as follows:  $R^6$  is  $-P(=R^9)R^{10}R^{11}$ .

The Applicants have amended the claims to limit the definition of  $R^6$  to cyano, boronic acid,  $-SO_2Z^1$ ,  $-P(=O)Z^1$ ,  $-C(=NH)NH_2$ ,  $-CH=NR^{12}$ . Consequently, the Applicants respectfully assert that the amended claims do not read on the compound disclosed in Natchev.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 102(b).

**Claim Rejections based on 35 U.S.C. § 103(a)**

Claims 13 and 14 stand rejected under 35 U.S.C. § 103(a) being unpatentable over Scheidt, in view of Remington's: the Science and Practice of Pharmacy, 19<sup>th</sup> edition, vol. 1, p. 806. The Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, a number of criteria must be met. For example, all of the limitations of a rejected claim must be taught or suggested in the prior art reference (or references when combined) relied upon by the Examiner; or they must be among the variations that would have been "obvious to try" to one of ordinary skill in the relevant art in light of the cited reference(s). Moreover, one of ordinary skill in the relevant art must have a reasonable expectation of success in light of the cited reference or combination of references. Importantly, the reasonable expectation of success must be found in the prior art, and may not be based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); see MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

The Applicants believe that the Examiner has failed to state a *prima facie* case of obviousness for the rejected claims, as the cited reference does not teach or render "obvious to try" each and every element of the amended claims.

The Examiner contends Scheidt discloses compounds of formula I (see above) which fall within the scope of the rejected claims. However, the amended claims do not read on the compounds disclosed in Scheidt. In the parlance of the structural limitations (i.e., formula I) of the rejected claims, the compounds disclosed by Scheidt contain an aldehyde group ( $-\text{C}(=\text{O})\text{R}^{12}$ ) in the position corresponding to  $\text{R}^6$ . In contrast,  $\text{R}^6$  in the amended claims is limited to cyano, boronic acid,  $-\text{SO}_2\text{Z}^1$ ,  $-\text{P}(=\text{O})\text{Z}^1$ ,  $-\text{C}(=\text{NH})\text{NH}_2$ , or  $-\text{CH}=\text{NR}^{12}$ .

Furthermore, based on the cited combination one of skill in the art would not have had a reasonable expectation of success in developing the claimed packaged pharmaceutical comprising a compound amended claim 1. The Scheidt compounds differ chemically from the claimed compounds. Further, the Scheidt compounds were shown to be effective as cysteine protease inhibitors to target parasitic diseases (e.g., malaria). In contrast, Applicants' claimed compounds are selective inhibitors of post-proline cleavage enzymes and are used to regulate

glucose metabolism. Thus, due to the differences between the structure and function of the compounds disclosed in Scheidt and those of the claimed compounds, one of skill in the art would not have had a reasonable expectation of success in developing the claimed packaged pharmaceutical based on the cited references.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 103(a).

**Claim Rejections – 35 U.S.C. § 112¶2**

The Examiner has rejected claims 1-7, 13 and 14 under 35 U.S.C. § 112, second paragraph, based on the contention that they are indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Specifically, the Examiner asserts that the identity of the structural variable L at different positions in formula I is ambiguous. The Applicants point the Examiner to page 18, lines 7-9 of the specification for clarification.

As used herein, the definition of each expression, e.g., alkyl, m, n, etc., when it occurs more than once in any structure, is intended to be independent of its definition elsewhere in the structure.

Solely to expedite prosecution, the Applicants have amended claim 1 to reflect that each instance of L is defined independently for each occurrence from among the listed definitions. The amendment was made merely for the sake of clarity, and does not reflect a change in the scope of the invention for which protection is sought.

Accordingly, the Applicants respectfully request the withdrawal of the rejection based on 35 U.S.C. § 112¶2.

**Fees**

The Applicants believe that they have provided for all required fees in connection with the filing of this Response. Nevertheless, the Commissioner is hereby authorized to charge any additional required fees to our Deposit Account, **No. 06-1448** reference **TUV-048.01**.

**Conclusion**

In view of the above amendments and remarks, it is believed that the pending claims are in condition for allowance. If a telephone conversation with the Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to contact the undersigned at (617) 832-1000.

Respectfully submitted,  
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